# Evaluation of Possible Changes in Intraocular Pressure and Optical Coherence Tomography Measurements in Severe OSAS Patients After 3 Month Positive Airway Pressure Treatment

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# Abstract

**Purpose:** To identify and compare possible changes in intraocular pressure (IOP), macular and peripapillary retinal nerve fiber layer (RNFL) thickness using optical coherence tomography (OCT) before and after 3 months of positive airway pressure (PAP) in patients with severe OSAS.

**Materials and Methods:** Twenty-five patients diagnosed with severe OSAS in the neurology sleep outpatient clinic were included in the study. Ophthalmologic examinations were performed at the time of diagnosis and after 3 months of PAP treatment. Statistical analysis of comparisons of IOP and OCT measurements taken before and after PAP treatment was performed. Before treatment, the correlations between central corneal thickness (CCT), body mass index (BMI), OCT, IOP and sleep parameters were statistically investigated.

**Results:** When comparisons were made for both eyes, after 3 months of PAP treatment, a statistically significant decrease in IOP, thickening of the macula, and thinning of RNFL in the superior nasal sector were found when compared with the measurements previously taken at the time of diagnosis ($p < 0.05$). There was no correlation between pre-treatment IOP, OCT, CCT, BMI and sleep parameters.

**Discussion:** The inflammatory effects of OSAS on the IOP and macula have been shown to be reversible with a 3-month PAP treatment, but the reversibility of the neurodegenerative effects of OSAS on RNFL with this treatment seems controversial. OCT is a promising technique for monitoring disease progression in patients with severe OSAS under PAP treatment.


# Introduction

Obstructive sleep apnea syndrome (OSAS) is a common sleep-related breathing disorder characterized by apnea-hypopnea episodes due to recurrent upper airway obstructions during sleep [1,2]. It has been associated with increased morbidity and mortality due to periodic oxygen desaturations and hypoxia episodes leading to intermittent hypoxemia and hypercapnia [3-5]. These pathophysiological changes are thought to cause an increase in intracranial pressure, sympathetic activation, impaired tissue oxygenation and oxidative stress, and as a result, cause various pathologies in the organs that involve the eye [6-8].

Optical coherence tomography (OCT) is an imaging technology that allows the macula and peripapillary retinal nerve fiber layer (RNFL) to be evaluated noninvasively [9]. Thickness measurements of the macula and RNFL with OCT reflect neurons and neuronal axons, respectively, and allow to measure neuronal loss and ganglion cell axonal loss, respectively [9]. Various ocular diseases such as ischemic optic neuropathy, central serous chorioretinopathy, retinal vein occlusion, floppy eyelid syndrome and papilledema have been associated with OSAS in the literature [10-12]. However, studies investigating the relationship between OSAS, intraocular pressure (IOP) and OCT measurements have conflicting results, and there are a limited number of studies investigating positive airway pressure (PAP) treatment on these parameters in patients with severe OSAS [13]. Therefore, this study aimed to identify and compare

possible changes in intraocular pressure, macular thickness, and RNFL thickness before and after 3 months of PAP in patients with severe OSAS.

# Methods

## Study Design

The study design is prospective, cross-sectional, performed after February 2021. It was prepared in accordance with the principles of the Declaration of Helsinki. University Research and Ethics Committee approval was obtained (ethics committee approval date-number: 05/02/2021-17). All individual participants gave written informed consent for inclusion in the study. Patients aged 18 and over who were diagnosed with “severe OSAS” with apnea-hypopnea indices (AHI) by polysomnography (PSG) in the sleep unit of the neurology clinic were included in the study. They were taken to the ophthalmology clinic twice to be examined before starting the treatment prescribed by the chest diseases department and after 3 months of treatment. All examinations were done by a single physician and all measurements were made by a single technician.

Exclusion criteria for all subjects include being an active smoker, a systemic disease other than OSAS, cerebrovascular disease, diabetes mellitus, dyslipidemia, hypertension, any ocular disease involving the anterior or posterior segment, and history of glaucoma, ocular trauma, ocular surgery, laser therapy, and intravitreal injection. In addition, subjects having abnormal examination findings such as visual acuity <20/20, refractive errors>2.00D, corrected IOP higher than 21mmHg, signs of retinopathy, vasculopathy and signs of optic nerve disease such as glaucomatous cupping were also excluded.

## Polysomnography

PSG tests of the subjects were conducted by Respirnics Alice 5, 55 channel polysomnograph, sleepware G3. A tracheal microphone on the neck was used to record snoring. Oxygen saturation was measured by a fingertip pulse oximeter. Airflow was measured using an oronasal thermistor. Respiratory movements of abdomen and thorax, body position, electroencephalogram, leg and submental electromyogram, sandelectro-oculogram and electrocardiogram were also recorded. All digitalized signals were saved by a personal computer. The American Academy of Sleep Medicine rules were followed in order to perform scoring [14].

A reduction of ≥ 3% in capillary oxygen saturation was defined as desaturation. An airflow interruption during sleep lasting at least 10 seconds was defined as apnea; whereas a decrease of ≥ 50% in airflow lasting ≥10 seconds with an arousal or a desaturation was defined as hypopnea. The number of hypopneas and apneas per hour of sleep were used to measure AHI. The oxygen desaturation index was calculated by dividing the scored number of desaturations by the bed-waking times (estimated sleep duration). Indices of nocturnal hypoxemia revealed by an analysis of mean oxygen saturation ($SaO_2$) and minimal SaO2 value noted during sleep. OSAS was identified when AHI was calculated 5. In accordance

with the AHI measurements, OSAS patients were categorized in 3 groups as “mild” who had 5< AHI ≤ 15, “moderate” who had 16≤ AHI ≤ 30, and “severe” who had AHI> 30 [15].

Sleep parameters obtained by PSG included AHI, mean saturation, minimum oxygen saturation, oxygen desaturation index (ODI), total desaturation times during sleep, sleep efficiency and sleep stages (non-REM and REM). The demographic data of the patients (age, sex), body mass index and Epworth sleepness scale results were recorded from their files. The treatment of patients with severe OSAS consisted of positive airway pressure (PAP) for 3 months [16]. In accordance with generally accepted principles, patients who received PAP treatment with> 70% of the overall duration of use and used devices for> 4 hours or more per night were included in the study.

## Ocular Examination

Patients with severe OSAS were examined by a single ophthalmologist (AIC) before OSAS treatment was initiated and after 3 months of PAP treatment given by a pulmonologist (ND). The patients underwent an ocular examination including visual acuity test (with a Snellen chart), slit-lamp biomicroscopy, funduscopy, gonioscopy and intraocular pressure (IOP) measurement by applanation tonometry. Central corneal thickness (CCT) of subjects was measured at the time of diagnosis by the same inspector (AIC) with a pachymeter (Canon Inc. fully automatic tonometer TX-20P, Tokyo, Japan).

## Optical Coherence Tomography Measurements

Analysis of RNFL thickness and macular thickness was performed using the OCT device (Cirrus ™ HD-OCT, Carl Zeiss Meditec, Inc). The average RNFL thickness and the thickness of four RNFL sectors (nasal, superior, temporal, inferior) including the four subregions of the RNFL sectors (nasal inferior, nasal superior, temporal inferior, temporal superior sectors) were obtained by 200 x 200 axial scanning of 6x6x2 $mm^3$ area around the optic nerve head. Each patient underwent three OCT scans with a macular 512x128 cube scan. Total average macula thickness measurements were noted.

All measurements were performed three times for each eye by the same operator (EK) between 10:00 and 12:00 hours. Each patient was scanned OCT at the time of diagnosis and 3 months after PAP treatment. The best quality scan with a signal strength of ≥8 was used for analysis. Scans with a signal strength≤7 and scans with any media opacity due to artefacts were excluded.

## Statistical analysis

In the present study, patients’ pretreatment measurements that were performed at the time of diagnosis and posttreatment measurements that were performed after PAP treatment that lasted for 3 months were analyzed. The correlations between pre-treatment measurements including OCT, IOP, CCT, BMI and sleep parameters were statistically analyzed. The data were analyzed using the SPSS 21 program with 95% confidence. Mean, standard deviation (minimum and maximum) values were used in the expression of continuous variables. After performing the Shapiro Wilk test for normality analysis, analyzes were

performed with Paired-t and Wilcoxon tests. Pearson and Spearman correlation tests were used in the analysis of the relationship between variables.

# Results

Twelve of 44 patients who were diagnosed with severe OSAS who were taken from the sleep unit were excluded from the study because they missed their follow-up at the 3rd month or the treatment was discontinued. Seven patients were excluded because they had at least one of the exclusion criteria. 50 eyes of the remaining 25 patients were analyzed. The mean age of the patients (12 females and 13 males) was 47.64 ± 12.42 years (range 24-65). The mean BMI of the patients at the time of diagnosis was 32.24 ± 4.07 (range, 25.3 - 40.3). The mean CCT of the patients at the time of diagnosis was 532 ± 21.94 (range, 482-566). The demographic characteristics and the pretreatment CCT values of the patients are given in **Table 1**. The sleep parameters of the patients obtained by PSG are given in **Table 2.** There was no statistically significant correlation found between the pretreatment measurements of patients including OCT, IOP, CCT, BMI and sleep parameters.

### Evaluation of intraocular pressure measurements

The evaluation of pretreatment and posttreatment measurements of IOP of patients with severe OSAS are shown in **Table 3**. It was observed that there was a decrease in the mean values of IOP in the patients after 3-months of PAP treatment, which were found close to the significant values when both eyes were evaluated. **(**17,12 ± 3,24 vs 16,3 ± 2,9, *p*=0,064). When the pretreatment and posttreatment IOP values of the right and left eyes were compared, separately, a significant decrease was observed in IOP of the left eyes after 3 months of PAP treatment (17,36 ± 3,26 vs 16,16 ± 2,93 (p=0,05)); while the comparative values of IOP in the right eyes were found statistically insignificant (16,88 ± 3,27 vs 16,44 ± 2,93, *p*=0,345).

### Evaluation of optical coherence tomography measurements

The pretreatment and posttreatment OCT measurements of patients with severe OSAS are shown in **Table 3.** When both eyes were evaluated together, a significant reduction in the thickness of superior nasal sector of RNFL was observed after treatment compared to the measurements made at the time of diagnosis before treatment (122.84 ± 19.54 versus 119.12 ± 20.97, $p = 0.038$). No significant change was observed in other RNFL sectors ($p > 0,05$ for all). Although the superior nasal sector of RNFL measured after treatment was found to be thinner than the pre-treatment measurements for both the right and left eyes, this difference was found to be close to significant values for the left eyes (127.36 ± 20.75 vs 124.96 ± 20.23, $p = 0.065$), it was found to be insignificant for the the right eyes (118,32 ± 17,5 vs 113,28 ± 20,45, p= 0,138).

When both eyes were evaluated together, a significant increase was observed in the mean macular thickness after PAP treatment compared to the values measured before treatment (292.56 ± 14.01 vs. 293.46 ± 14.47, $p = 0.031$). However, while this difference was statistically insignificant for the right eyes

(292.88 ± 13.46 vs 293.4 ± 13.77, $p$ = 0.306), it was significant for the left eyes (292.24 ± 14.82 vs 293, 52 ± 15, 42, $p$ = 0.050).

# Discussion

Recurrent episodes of apnea or hypopnea due to partial or complete upper airway obstruction during sleep are associated with hypercapnia and hypoxia, leading to impaired sympathetic activity, irregulation of cerebral and ocular blood flow, and disruption of the balance between vasomeditors such as nitric oxide, vascular endothelial growth factor, and endothelium [17-20]. In addition, it has been suggested that the disturbance of the balance between these vasomediators causes an increase in intracranial pressure, which contributes to a decrease in cerebral perfusion and impaired ocular blood flow [21-24].

It has been shown that the neurosensory retina, especially the retinal ganglion cells forming the optic nerve head, is hypersensitive to hypoxia and reduced perfusion [25]. Hypoxia and hypoperfusion have been important triggering factors for inflammation in the nuclear cell membrane and an increase in oxidative stress, leading to impairment of the cell membrane and cellular edema and subsequently resulting in apoptosis seen in the latter stages of hypoxic diseases [26,27]. These alterations in the brain and the orbita lead to papilledema that reflects the increase in RNFL thickness at early stages of the disease which proceeds to neuronal degeneration and apoptosis that later presents as thinning of RNFL in OCT measurements [27,28]. Therefore RNFL thinning has been suggested as the resulting neurodegenerative effect of OSAS in ocular structures [9, 29, 30].

Increasing evidence has shown that the longer the duration of oxygen desaturation, the more severe the disease on the optic nerve, thus the thinner the RNFL become [13,22]. Based on this fact, the current study aimed to establish the effects of PAP treatment on RNFL and macula of patients with severe OSAS by using OCT to understand if the effects of OSAS related hypercapnia and hypoxia on these parameters were reversible by PAP treatment or not. Following a 3-months PAP treatment, thickening of macula as well as thinning of RNFL in the superior nasal sector was found in comparison with OCT measurements taken before treatment. While it was thought that hypoxia-induced inflammation may regress with PAP treatment and a significant improvement in macular thickness can be observed, changes in the upper nasal sectors of the RNFL appear to be irreversible even with an intense PAP given for 3 months.

On the other hand, the effects of both local inflammatory reactions and increased intracranial pressure may have affected RNFL, which initially appeared as thickening in some sectors in the early stages. (9) In connection with this fact, increased intracranial pressure and papilledema in patients with OSAS have been reported to improve after PAP treatment, which may imply that oxygenation therapy through PAP treatment may be effective in the early stages of the disease to reverse the edematous effects of OSAS [31,32]. Accordingly, thinning in the superior nasal sector of RNFL may have occured due to reversible edematous changes at early stages of the disease that recovered after 3-months of PAP treatment. However, the thinning in the superior nasal sector of the RNFL may have also occured due to neurodegeneration developed after irreversible retinal ganglion cells' axonal loss caused by the acute

onset of inflammation, intracranial pressure and hypoxia as retinal ganglion cells are sensitive to even mild hypoxemia [25-28]. Consistent with these findings, O'Donoghue et al showed that after 6 months of PAP treatment, 23 patients with severe OSAS showed a significant reduction in whole brain volume of approximately 4% in high-resolution magnetic resonance scanning brain imaging [32].

It was noteworthy that in this study, thinning seen only in the upper nasal sector of RNFL was not seen in other sectors. This can be attributed to the difference between RNFL sectors in terms of vascularization; This suggests that the duration of the resulting neurodegenerative effect of OSAS on RNFL sectors may also differ. It has been shown that the temporal RNFL has been shown to be more vascularized than the nasal RNFL in young and healthy individuals [33,34]. Therefore, temporal RNFL is thought to be less susceptible to hypoxemic stress as well as to intracranial hypertension caused by hypoxic and hypercapnic episodes of OSAS. Indeed, in a meta-analysis including 10 studies that analyzes a large sample of OSAS patients with healthy controls, it was found that RNFL in OSAS patients had thinning mostly in the mean, upper, nasal and lower sectors [13].

Glaucomatous optic neuropathy is characterized by axonal loss of ganglion cells and visual field defects over the years, which can first be noticed by the thinning of RNFL measured by OCT. (35) Thinning of RNFL in OSAS patients has been associated with a high prevalence of primary open angle glaucoma among OSAS patients in some studies [29,36]. Similar to the pathogenesis of OSAS, the impaired balance between vasodilators such as nitric oxide and vasoconstrictors such as endothelin is considered one of the causes of glaucoma development [37]. Therefore, it is suggested that this mechanism is the cause of glaucoma-like damage resulting in damage to retinal ganglion cells in patients with OSAS. Based on these facts, the present study also investigated the effect of PAP treatment on IOP in patients with severe OSAS, where it was shown that PAP treatment caused a statistically significant IOP reduction in both eyes. Similar to the current study, Casas et al included patients with OSAS without any glaucomatous evidence, such as IOP values >21 mmHg, abnormal gonisoscopy, and abnormal perimetric findings, in order to evaluate the thinning of RNFL seen in OSAS patients [9]. They showed significantly higher IOP values and changes in the visual field index of OSAS patients compared to controls. They also found an increase in some optic nerve head parameters in OSAS patients without glaucoma compared to healthy controls, which were considered signs of neuronal degeneration. As a matter of fact, a positive correlation between IOP and AHI has been shown among OSAS patients in previous studies [38, 39].

There are only a few studies evaluating IOP, macula, and RNFL of patients with severe OSAS before and after PAP treatment [40,41,42]. Batum et al. investigated the effects of 6-month PAP treatment on patients with severe OSAS [40]. Similarly, the authors reported a significantly thicker macula in the foveal area after treatment compared to OCT measurements at diagnosis. They stated that other sectors of the macula were also measured thicker after PAP treatment, but these differences were not found to be statistically significant. Similar to the pathophysiology seen in RNFL, the authors attributed these changes in macular thickness to the effects of PAP treatment, which increased patients' oxygen saturation to counteract the inflammatory effects associated with hypoxia. However, in contrast to the current study, Batum et al found a significant increase in the average, nasal, and inferior sectors of RNFL

thickness after 6 months of PAP treatment compared to thickness measurements at the time of diagnosis. In addition, the authors stated that PAP was effective in preventing hypoxia in retinal tissues, although it did not cause any change in intraocular pressure in patients with severe OSAS. Supporting this finding, the authors reported significant changes in visual evoked potential testing in patients with severe OSAS after PAP treatment, indicating that the axonal and myelin component of the optic nerve was damaged by recurrent microischemia due to intermittent hypoxemia [30,43].

In contrast to the current study and the study of Batum et al., Yuvacı et al. reported significantly thinner macula in the superior, superior nasal, inferior nasal and temporal superior sectors measured after 3 months of PAP treatment compared to the measurements at the time of diagnosis [41]. Differently, they evaluated only the right eyes of patients with severe OSAS. The authors also found that after 3 months of PAP treatment, RNFL thickness was significantly reduced in the average, inferior, superior nasal, and superior temporal quadrants, but noted that clinical improvement was observed in patients with severe OSAS. The researchers also noted that the average RNFL thickness decreased after both 4 weeks and 12 weeks of PAP treatment. Also, unlike the current study, Yuvacı et al. showed a statistically significant increase in mean IOP that did not reach a normal range after PAP treatment. Nevertheless, RNFL thinning was attributed not only to glaucoma, but also to apnea-hypopnea induced hypoperfusion and ischemia, vasomediator imbalance such as an imbalance between NO and endothelin, and nocturnal hypotension [41].

Zengin et al. demonstrated changes in RNFL thickness after one year of follow-up in mild, moderate, and severe OSAS patients [42]. Similar to the study of Yuvacı et al., after 12 months of PAP treatment, they showed thinning of the RNFL in the measurements of the average, inferior nasal, superior nasal, and superior temporal sectors. They also observed a progressive reduction in RNFL thickness during follow-up, which was shown to be statistically insignificant compared to healthy controls. The study of Zengin et al., unlike the current study and the studies mentioned above, consisted of 44 OSAS patients, including only 14 severe OSAS patients. In addition, Zengin et al. showed a statistically significant increase in the mean IOP of OSAS patients during the course of the disease, in contrast to the decrease in IOP levels of OSAS patients after 3 months of PAP treatment. The authors concluded that the thinning observed in RNFL could be caused by both glaucoma and OSAS [42].

Indeed, a relatively high incidence of glaucoma in OSAS patients has been documented in the literature [36]. However, studies investigating the relationship between glaucoma and OSAS still reveal conflicting results. While some studies associated normotensive glaucoma or primary open angle glaucoma with OSAS [29,36, 38,39,44,45]; some studies did not find any correlation between OSAS and glaucoma, or some studies found similar prevalence of glaucoma in OSAS patients compared to normal subjects [22,46, 47, 48,49]. In addition, there are reports in the literature documenting improvement of visual defects in OSAS patients following PAP treatment [50,51]. Further, the thinner RNFL in patients with OSAS without optic neuropathy symptoms or visual field defects suggests that OSAS may have an effect on the optic nerve for other reasons, but not glaucoma [9,30]. The diversity of all these results and interpretations in the literature can be attributed to patients who differ in terms of OSAS severity and

duration, as well as study design, sample size and demographic characteristics. Therefore, we believe that further studies with large homogeneous groups are needed to establish the relationship between intraocular pressure and OSAS and to distinguish RNFL changes from glaucoma changes.

The greatest strength of this study is that all patients with OSAS are free from other known diseases and have never received sleep apnea treatment before. On the other hand, the most important limiting factor of the study was the relatively small sample size and the lack of long-term follow-up (longitudinal design) of patients with severe OSAS. In addition, since a vascular pathogenesis or change has been mentioned in the pathogenesis of the neurodegenerative effects of OSAS, the fact that brain and ocular vascularity have not been measured by imaging and measurement techniques such as OCTA or MRI can be considered as a deficiency.

Our study is important because it is one of the few studies evaluating the effectiveness of PAP treatment on IOP, macula, and RNFL in patients with severe OSAS. The effects of OSAS on IOP and macula have been shown to be reversible with a 3-month PAP treatment, but the reversibility of the neurodegenerative effects of OSAS on RNFL with this treatment still seems controversial. In summary, the findings of this study suggest that OCT measurements will be candidates for use as a biomarker to evaluate disease progression in patients with severe OSAS under PAP treatment. However, as this issue has not been investigated in depth in the literature, future studies with a longitudinal design and larger sample size are needed to distinguish the effects of OSAS and PAP treatment on IOP, macula, and RNFL.

# Declarations

### Author contributions

ND and AIC and SU contributed to writing original draft preparation; SU and ND contributed to conceptualization; AIC contributed to formal analysis and investigation; ND and SU contributed to methodology; AIC and ND contributed to writing—review and editing; AIC contributed to the provision of resources; AIC, ND and SU contributed to supervision.

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### Conflict of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

### Ethical Approval

All procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration

and its later amendments or comparable ethical standards (ethics committee approval date- number: 05/02/2021-17).

### Informed Consent

Informed consent was obtained from all individual participants included in the study.

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# Tables

**Tablo.1** Demographic characteristics of patients with severe OSAS and central corneal thickness measurements before treatment

| | |
|---|---|
| **Age (years) (range)** | 47.64 ± 12.42 (24-65) |
| **Gender** | |
| **Female** | 12 |
| **Male** | 13 |
| **BMI (mean ± SD) (range)** | 32.24 ± 4.07 (25.3-40.3) |
| **CCT (mean ± SD) (range)** | 532 ± 21.94 (482-566) |

**Table 2.** Values of pretreatment sleep parameters

| Sleep parameters | Mean ± SD (range) |
|---|---|
| Apnea-hypopnea index | 59,76 ± 26,58 (29,6-126,4) |
| Minimum oxygen saturation | 76,8 ± 6,75 (60- 85) |
| Mean oxygen saturation | 92,24 ± 2,33 (87- 96) |
| Desaturation time (minute) | 32,07 ± 44,07 (0,9-167,2) |
| Oxygen desaturation index | 36,82 ± 25,39 (7-108,2) |
| Efficancy of sleep | 78,33 ± 9,76 (59,4-98) |
| Non-REM Stage 1 (%) | 24,6 ± 12,03 (8,8-53,7) |
| Non-REM Stage 2 (%) | 55,78 ± 11,26 (36,3-82,6) |
| Non-REM Stage 3 (%) | 12,12 ± 9,66 (0-36,1) |
| REM (%) | 6,93 ± 6,34 (0-24,2) |

SD: standart deviation; REM: rapid eye movement phase of sleep

**Table 3.** Evaluation of intraocular pressure measurements and optic coherence tomography measurements of patients with severe OSAS

| **Intraocular Pressure (mmHg)** | | **Both Eyes (Mean ± SS)** | **p** | **Right Eyes (Mean ± SS)** | **p** | **Left Eyes (Mean ± SS)** | **p** |
|---|---|---|---|---|---|---|---|
| Mean | Pretreatment | 17,12 ± 3,24 | 0,064 | 16,88 ± 3,27 | 0,345** | **17,36 ± 3,26** | **0,050** |
| | Posttreatment | 16,3 ± 2,9 | | 16,44 ± 2,93 | | **16,16 ± 2,93** | |
| **RNFL Thickness Quadrants (µm)** | | **Both Eyes (Mean ± SS)** | **p** | **Right Eyes (Mean ± SS)** | **p** | **Left Eyes (Mean ± SS)** | **p** |
| Average | Pretreatment | 107,14 ± 10,54 | 0,446 | 107,56 ± 10,37 | 0,226 | 106,72 ± 10,91 | 0,718 |
| | Posttreatment | 107,42 ± 10,63 | | 108,28 ± 10,27 | | 106,56 ± 11,13 | |
| Superior | Pretreatment | 134,44 ± 16,71 | 0,363 | 132,48 ± 16,94 | 0,840 | 136,4 ± 16,58 | 0,178 |
| | Posttreatment | 133,7 ± 17,66 | | 132,2 ± 18,45 | | 135,2 ± 17,08 | |
| Inferior | Pretreatment | 136,94 ± 18,56 | 0,301 | 137,68 ± 17,66 | 0,364 | 136,2 ± 19,77 | 0,508 |
| | Posttreatment | 138,1 ± 17,18 | | 138,68 ± 17,15 | | 137,52 ± 17,55 | |
| Temporal | Pretreatment | 76,74 ± 11,55 | 0,085 | 78,32 ± 12,13 | 0,404 | 75,16 ± 10,96 | 0,133 |
| | Posttreatment | 77,34 ± 11,64 | | 78,68 ± 12,06 | | 76 ± 11,28 | |
| Nasal | Pretreatment | 80,66 ± 17,08 | 0,481 | 82,52 ± 18,15 | 0,547 | 78,8 ± 16,1 | 0,702 |
| | Posttreatment | 81,32 ± 16,61 | | 83,6 ± 17,04 | | 79,04 ± 16,19 | |
| Superior Temporal | Pretreatment | 148,26 ± 19,5 | 0,412 | 150,96 ± 17,13 | 0,564 | 145,56 ± 21,62 | 0,478 |
| | Posttreatment | 147,5 ± 21,17 | | 149,96 ± 20,97 | | 145,04 ± 21,52 | |
| **Superior Nasal** | Pretreatment | **122,84 ± 19,54** | **0,038** | 118,32 ± 17,5 | 0,138 | 127,36 ± 20,75 | 0,065 |
| | Posttreatment | **119,12 ± 20,97** | | 113,28 ± 20,45 | | 124,96 ± 20,23 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Inferior Temporal | Pretreatment | 151,34 ± 22,23 | 0,154 | 152,32 ± 21,14 | 0,364 | 150,36 ± 23,66 | 0,099 |
| | Posttreatment | 152,98 ± 24,13 | | 154,32 ± 24,4 | | 151,64 ± 24,29 | |
| Inferior Nasal | Pretreatment | 121,7 ± 22,7 | 0,783 | 122,44 ± 21,2 | 0,720 | 120,96 ± 24,53 | 0,981 |
| | Posttreatment | 122,02 ± 18,72 | | 123,04 ± 18,77 | | 121 ± 19 | |
| **Macula Thickness (µm)** | | **Both Eyes (Mean ± SS)** | **p** | **Right Eyes (Mean ± SS)** | **p** | **Left Eyes (Mean ± SS)** | **p** |
| Mean | Pretreatment | **292,56 ± 14,01** | **0,031** | 292,88 ± 13,46 | 0,306 | **292,24 ± 14,82** | **0,050** |
| | Posttreatment | **293,46 ± 14,47** | | 293,4 ± 13,77 | | **293,52 ± 15,42** | |

**Wilcoxon test; RNFL: peripapillary retinal nerve fiber layer